UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/070,719	09/20/2002	James Robl	103080-P08-058	2839

1473 7590 12/05/2008

ROPES & GRAY LLP
PATENT DOCKETING 39/361
1211 AVENUE OF THE AMERICAS
NEW YORK, NY 10036-8704

EXAMINER	
TON, THAIAN N	
ART UNIT	**PAPER NUMBER**
1632	

MAIL DATE	DELIVERY MODE
12/05/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/070,719	ROBL ET AL.	
	Examiner	Art Unit	
	Thaian N. Ton	1632	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *01 August 2008*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *51,52 and 54-58* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *51,52 and 54-58* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Applicants' Response, filed 8/1/08, has been entered. Claims 51, 52, 54-58 are pending and under current examination.

Double Patenting

Claims 51, 52, 54-58 stand provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1, 40-41 of copending Application No. 10/922,374. Applicants provide no specific arguments for this rejection other than the rejection be held in abeyance until allowable subject matter is determined. Accordingly, the rejection is maintained. The claims of the '374 case produce a blastula or morula by insertion of a desired human cell or cell nucleus. Thus, introduction of an entire human cell would encompass introducing mtDNA into the enucleated oocyte.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 51, 52, 54-58 stand rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Applicants Arguments. Applicants argue that the claims do not require that a blastua or morula of the invention produce true ES cells, and that the specification teaches that the cells produced by the methods of the Application may be embryonic or ES-like, and that the term "like" indicates that the cells are not necessarily ES cells and may resemble them, such as by morphology, and that one of ordinary skill would understand this to be the case. Therefore, Applicants argue, the cells produced by the methods of the Application may, but do not have to, meet the requirements of a true ES cells, such as a normal karyotype, as stated by the Examiner. See p. 5 of the Response.

Response to Arguments. These arguments have been fully considered, but are not persuasive. The specification as a whole does not contemplate utilizing a cell with only ES-like morphology in the use of the contemplated methods. That is, the specification does not provide any guidance for a cell that does not have the art-recognized characteristics, but merely some characteristics of an ES cell, and further, the specification provides no enabled use for such a cell. The specification does not teach which characteristics must be present for a cell to be "like" an ES cell, such that this cell could be used in any of the methods that are contemplated by the specification. The specification clearly discusses the art-recognized properties of ES cells, and contemplates using the ES or ES-like cells of the claimed invention to produce transgenic embryonic or differentiated cells, cell lines, tissues, or as donor cells in NT methods to produce cloned or chimeric animals (p. 2, lines 1-5). The specification clearly uses the term "ES-like" or "stem cell like" cells to describe cells that have characteristics, such as the differentiation capacity and pluripotency of ES cells. The specification teaches that the cells of the invention are referred to as "stem-like" cells because of the manner in which they are produced, but that these cells "are expected to possess similar differentiation capacity as normal stem cells." See p. 17-18, bridging sentence, of the specification. That is, it is clear that the specification does not define a cell as "stem-like" or "embryonic-

stem like" merely because it has one characteristic similar to an ES cell, the specification clearly contemplates that these cells would have similar differentiation capacities as a normal ES cell and possess other art-recognized properties of an ES cells.

Applicants' Arguments. Applicants argue that although there is a low-efficiency in producing interspecies NT units, this does not evince unpredictability or undermine enablement, because the experimentation would not be undue. Applicants argue that the methods taught by the instant application are predictable and reproducible, as evidenced by Chang *et al.*, because Chang show cross-species NT by inserting human somatic nuclei into bovine oocytes, using the same methods as instantly-filed disclosure, therefore, Applicants argue, Chang supports Applicants' contention that the claimed invention is enabled. See pages 7-8 of the Response. Applicants argue that the cells produced by the methods of the invention may be used to study differentiation and for assay purposes, and that the Application does contemplate other uses for cells by blastula or morula and never asserts that the only use of the claimed methods is the production of ES cells. Although a specific differentiation potential is not shown for the claimed cells, one of ordinary skill in the art would believe that the cells with ES-like morphology would have some differentiation potential and can be used to study differentiation. See pp. 6-7 of the Response.

Response To Arguments. These arguments are considered, but are not persuasive. The claims are specifically directed to methods of producing blastula or morula. The Examiner responds that that the standard, under 112, 1st paragraph is to teach the skilled artisan how to make and use the claimed invention. Applicants elected a method of producing embryonic or stem-like cells produced by their claimed methods. Although the claims recite the production of a morula or blastula, there is no other enabled use that is contemplated by the specification within Applicants' election, other than to produce embryonic or stem-like cells. That is,

even if one of skill in the art were able to produce morula or blastula stage embryos utilizing Applicants' methods, one of skill in the art would have to practice undue experimentation to use the claimed invention for its contemplated purpose, within Applicants' elected invention, which is to produce embryonic or stem-like cells. Additionally, given that only one NT unit was produced, and no ES cells were produced from this NT unit, one of skill in the art could not rely upon the state of the art of producing ES cells to enable the claimed invention. There is no other use that is enabled for producing a morula or blastula embryo in the context of Applicants' invention; therefore, the rejection of record is maintained. See also, Roach & McNeish and Thomson (cited previously) with regard to the unpredictability in the art of producing embryonic stem cells.

With regard to the Chang reference, the Examiner responds that although Chang teach the production of blastocyst stage embryos, many of the blastocysts had abnormal number of chromosomes, and even in light of the production of normal embryos, it is clear that Chang *et al.* show that cross-species NT is an unpredictable process. As stated previously, using a blastocyst with an abnormal karyotype to produce an ES cell with an abnormal karyotype is not within the definition of an ES cell (see Pera and NIH document, cited previously). There is no specific guidance provided by the specification or art of record, with regard to isolating embryonic or stem-like cells from morula or blastula that fulfill the art-recognized characteristics and definition of ES cells.

Additionally, there is no guidance in Chang to enable the claimed invention, because at the very most, they teach producing a blastocyst by interspecies nuclear transfer. They do not teach the production of embryo-derived proliferating cells that have an ES-like morphology. They state that the interspecies embryos had characteristics similar to bovine embryos. See p. 1386, col. 2, 1st full ¶. They do not discuss their cells, with regard to any differentiation capacity; in fact, they state that, "It was not determined whether the presence of human chromosome

complements with bovine mtDNA would secure the normality of pluripotent cells derived from interspecies embryos. Furthermore, there is no information on the normality of derivative tissues from interspecies embryos in which both human and bovine mtDNAs were heterogenetically present. Therefore, the presence of bovine mtDNA with human chromosomes in an embryo could cause metabolic disorders and alter cell properties of embryonic cells, if both are concomitantly inherited in inner cell mass cells." See p. 1387, 1st full ¶.

The Examiner maintains that the specification generally teaches the claimed method steps, but does not provide an enabling disclosure for the claimed invention. In particular, in light of the lack of an enabled use for the morula or blastula stage embryo produced by the claimed methods, as well as the unpredictability in the art with regard to the production of abnormal blastocysts in cross-species nuclear transfer, the lack of working examples provided, it would have required undue experimentation for one of ordinary skill in the art to practice the claimed invention.

Applicants point to p. 14, lines 9-11 for support to show that the cells produced by the methods may be used to study differentiation and for assay purposes. See p. 6-7 of the Response. The Examiner responds that although this citation discusses using the cells for differentiation studies or assay purposes, this citation requires the embryonic or stem-like cells, not the actual morula or blastula NT unit as claimed. It is reiterated that the skilled artisan, given the teachings of the specification, would clearly understand that the cells of the invention are embryonic or ES-like cells and would therefore have ES cell properties.

Applicants' Arguments. Applicants argue that the benefits of introducing mtDNA do not necessarily require incorporation of the DNA into the oocyte. Even if long term stability of donor-derived mtDNA is in doubt in a particular species, Chang provides guidance to show that the short term stability of donor-derived mtDNA is undisputed, and that it is apparent from the prior art in the field that

incompatibility with the nucleus with mitochondria during interspecies SCNT completes cloning, and thus, that supplementing SCNT procedures may be useful for improving cloning methods. Applicants conclude that the claimed invention is enabled for its breadth because the post-filing art supports their invention, and that the tools available to the skilled artisans permitted the practice of the claimed invention without undue experimentation. See page 6 of the Response.

Response to Arguments. These arguments are not persuasive. This is not persuasive. The arguments of counsel cannot take the place of evidence in the record. See *In re* Schulze, 346 F.2d 600, 602, 145 USPQ 716, 718 (CCPA 1965) and MPEP §716.01. Applicants have not provided an appropriate affidavit or declaration supporting that supplementing SCNT procedures improves cloning methods. The Examiner asserts that the prior art of record clearly shows that cross-species nuclear transfer is unpredictable (see Wolfe, Gurdon, Meirelles, Dominko, Dominko (1999)), and further, that the introduction of mtDNA is unpredictable with regard to the further development of the NT unit (see Jiang and Chen). Thus, these unpredictibilities, coupled with the lack of an enabled use of the morula or blastula stage NT unit, fail to enable the claimed invention. The post-filing art of Mastromonaco *et al.* show that even between close species, cross-species SCNT is highly unpredictable, see p. 4, 1st full ¶.

The specification is not enabling for the breadth of the claimed invention. The specification fails to overcome the above-recited unpredictibilities in cross-species nuclear transfer, the unpredictability in maintenance of the donor mtDNA, the importance of mtDNA in embryonic development, as well as in the production of embryonic or ES-like cells. One of skill in the art would not be able to practice the claimed invention, as broadly claimed, because the specification fails to provide guidance to practice the claimed invention, and the art provides significant teachings of the unpredictability found in the art, with regard to cross-species NT, and producing ES cells from the resultant NT unit. Because the intended use of the

claimed method is to produce embryonic stem cells, one of skill in the art would recognize that the NT unit would need to be able to develop to blastocyst stage, with the expression of appropriate markers and karyotype, in order to produce ES cells. The specification provides no other enabled use for the morula or blastula, produced by the NT method, within the context of Applicants' claimed invention. Accordingly, it is maintained that it would have required undue experimentation for one of ordinary skill in the art to practice the claimed invention.

Conclusion

No claim is allowed.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Thaian N. Ton whose telephone number is (571)272-0736. The examiner can normally be reached on 9-5:30 M-F.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Peter Paras can be reached on 571-272-4517. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Thaian N. Ton/
Primary Examiner, Art Unit 1632